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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,472	10/04/2005	Masashi Ito	082368-001500US	8056

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,472	ITO ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicant's response of December 19, 2006, to the non-final action dated August 29, 2006 has been entered. Claims 1, 2, 6 and 9 have been amended. No claims were cancelled or newly added. Claims 1-11 and 17 are pending in the application and under current examination.

New Claim Objections

Claims 1, 2, 5, 6, 7 and 9 are newly objected to because of the following informalities: the claims have not been amended to recite the elected species of the invention, insulin and retroviral vector; and encompasses non-elected subject matter, i.e. a broad variety of secreted proteins, that include GLP-1 and adeno-associated viral vector. Appropriate correction is required.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 1-7 and 9-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous office action dated August 29, 2006.

In view of Applicants' amendments of claim 1 to recite a foreign DNA operably linked to a promoter sequences, and claim 6 to recite establishing a primary culture, the previous rejection is hereby withdrawn.

Response to Claim Rejections - 35 USC § 102

Claim 1-9 and 17 stand rejected under 35 U.S.C. 102(e) as being anticipated by Furcht et al. (of record). In view of Applicants' amendments, directing the method claims to isolating adipocytes and establishing a primary culture, the previous rejection of claims 6 and 7 is hereby withdrawn. However, claims 6 and 7 are subject to separate rejection over the prior art, as set forth below. The rejection set forth on pp. 3-4 of the previous office action dated August 29, 2006 is maintained for claims 1-5, 8-9 and 17 for reasons of record and the following commentary.

Applicants traverse the rejection, arguing that the claims have been amended to set forth that the adipocyte(s) of the present invention are isolated and established from adipose tissue, that is in contrast from the stem cells by Furcht, which are derived from bone marrow. Applicants' arguments have been fully considered, but are not found persuasive.

Claims 1-5, 8-9 and 17 are directed to an adipocyte, or a primary cultured adipocyte, or an implant composition comprising the same. As such, the claims are directed to the product (i.e. the adipocyte), and not the process of making the product. There is no evidence that adipocytes established from adipose tissue are structurally or functionally different from those established from differentiated mesenchymal stem cells. As stated in MPEP 2113: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Thus, the rejection of claims 1-5, 8-9 and 17 is maintained for reasons of record and the preceding discussion.

Response to Claim Rejections - 35 USC § 103

Claims 9-11 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (of record), in view of Crystal et al. (of record), and further in view of Baetge et al. (of record). The rejection set forth on pp. 5-6 of the previous office action dated August 29, 2006 is maintained for claims 9-11 for reasons of record and the following commentary.

Applicants traverse the rejection, arguing that the combined disclosures of Furcht, Crystal and Baetge do not teach or suggest all of the claims limitations. That the primary reference Furcht does not teach the implant composition of the present invention, which requires a primary cultured adipocyte which is isolated and established from adipose tissue, and the disclosures of Crystal and Baetge do not supply the elements missing from Furcht. Applicants additionally argue that, the present invention, by employing primary cultured adipocytes isolated and established from adipose tissue, provides advantages over the cited art by providing a highly

homogenous population of adipose cells that are more easily isolated. Applicants' arguments have been fully considered, but are not found persuasive.

The response to arguments directed to the reference of Furcht et al. regarding the origin of the adipocytes has been addressed in the discussion above. Applicants' additional arguments regarding the homogeneity of the cells or their ease of isolation are irrelevant to the instant claims, as claims 9-11 are composition claims directed to adipocytes that are not structurally distinguishable from those described by Furcht et al. Thus, the rejection of claims 9-11 is maintained for reasons of record and the preceding discussion.

New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 6-7 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999), in view of Hertzel et al. (J. Lipid Res. 41:1082-1086; 2000).

Furcht et al. describe genetically modified adult stem cells that may be cultured and differentiated into adipocytes, for gene therapy, (Abstract). The isolation of the bone marrow derived mononuclear cells is described in Example 1(column 44), and their differentiation into adipocytes is outlined in Example 2 (column 46). Adipocytes derived from the stem cells can be used for the treatment of Type II diabetes (column 25). Furcht et al. specifically describe a number of secreted genes that may be used for gene therapy of diabetes (column 30). Additionally described are viral transfer vectors, including retroviruses (column 32). Retroviral vectors are extensively described in column 35. The transduction of marrow derived stem cells with retroviral vectors encoding eGFP is described in Example 4 (column 48).

Following *in vitro* culture and gene transfer, the transfected cells may be introduced locally or infused systemically (column 30). Specific examples of engraftment by intramuscular injection or stereotaxic transplantation into mice are described in Example 10 (columns 54-55). Furcht et al. further teach that the genetically altered stem cells can also be encapsulated in an inert carrier to allow the cells to be protected from the host immune system while producing the secreted protein (column 31). A number of pharmaceutically acceptable inert carriers materials, that include polymers and capsules are described in column 31. With specific reference to

treatment for diabetes, the authors state that autologous stem cells that have been genetically altered with a retroviral vector to produce insulin at physiologically therapeutic levels can be encapsulated for delivery within the patient's tissues, to produce insulin for extended periods of time (column 31). Furcht et al. further describe stem cells transfected with factor IX, that secrete the protein for at least 8 weeks after infusion into mice (column 30).

While Furcht et al. do not describe the establishment of their cultured adipocytes from adipose tissue, the culture of primary adipocytes from adipose tissue for gene transfer was well known in the art, as described by Hertzel et al., (second column, p. 1082), who describe the *in vitro* adenoviral transfer of a reporter gene via an adenovirus vector to primary murine adipocytes (Abstract). The authors additionally reference the *in vitro* transfection of rat and human adipocytes by other researchers (first column, p. 1083).

Therefore, a person of ordinary skill in the art would have been motivated to combine the teachings of Furscht et al. and Hertzel et al. and to substitute primary cultured adipocytes for differentiated adipocytes as a matter of design choice, and to forego the isolation and differentiation of mesenchymal stem cells (as indicated in Applicants' arguments).

A person of ordinary skill in the art, having applied the retroviral mediated gene transfer method of Furcht et al., to primary cultured adipocytes, as taught by Hertzel et al. would be able to practice the instantly claimed method of the invention, with a reasonable expectation of success. Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to substitute primary cultured adipocytes for the differentiated adipocytes of Furscht et al. at the time of the instant invention.

Conclusion

Claims 1-11 and 17 are not allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER